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Kinetics of Mixed Venous CO_2 Pressure in Incremental-Load Exercise

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Abstract. The purpose of the present study was to examine the kinetics of mixed venous CO_2 pressure ($P\bar{v}_{CO_2}$) in incremental-load exercise. $P\bar{v}_{CO_2}$ seemed to indicate a linear increase after a somewhat slow increase. CO_2 store phase appearing in expiration of CO_2 (stored CO_2) was calculated from the data of O_2 uptake ($\dot{V}_{O_2}$), CO_2 output ($\dot{V}_{CO_2}$) and work rate. The stored CO_2 indicated a linear increase after a time delay. The stored CO_2 also significantly related to $P\bar{v}_{CO_2}$. When kinetics of $P\bar{v}_{CO_2}$ at light exercise intensity was supposed from stored CO_2, $P\bar{v}_{CO_2}$ seemed to indicate a linear increase with a time delay. Excessive expired CO_2 (excess CO_2) was calculated from the data of $\dot{V}_{O_2}$ and work rate. The excess CO_2 significantly related to the increase of blood lactate. The blood lactate seemed to start to increase at around 1080 kpm/min. In spite of this change, a linear increase of $P\bar{v}_{CO_2}$ was unchanged. This result was considered to be related to the excessive CO_2 expiration corresponding to the increase of blood lactate. Thus, within the present results and assumptions, it seemed that $P\bar{v}_{CO_2}$ indicated a linear increase with a time delay without the effect of lactate increase in incremental-load exercise.

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Keywords: mixed venous CO_2 pressure, blood lactate, stored CO_2, excess CO_2

Introduction

The kinetics of mixed venous CO_2 pressure ($P\bar{v}_{CO_2}$) has been studied in human during exercise. Namely, when being indirectly measured in the constant-load exercise, it was reported that the $P\bar{v}_{CO_2}$ indicated almost no change from the resting value for a few seconds at the onset of exercise, then increased up to the new steady state value (Edwards et al., 1972). Thereafter, when being directly measured using pulmonary artery catheterization, the $P\bar{v}_{CO_2}$ was reported to indicate something of an increase even at a very early phase (Casaburi et al., 1989). Besides, Yano et al. (1995) pointed out that the later increase of $P\bar{v}_{CO_2}$ overshot when exercise intensity was high from the former reports (Cerretelli et al., 1966; Davies et al., 1972; Yano, 1986), and examined whether this overshoot was related to early lactate produced at the onset of exercise. The result was that the effect could not be observed at least when increase of blood lactate was low.

In incremental-load exercise, the beginning phase of constant-load exercise continuously appears in response to increase of work load so that $P\bar{v}_{CO_2}$ is considered to increase continuously during the exercise. It is also known that blood lactate starts to increase above a certain load in the incremental-load exercise (Beaver et al., 1986 a, b). Accordingly, in the incremental-load exercise, the effect of blood lactate may overlap with increase of $P\bar{v}_{CO_2}$ due to increase of work load. Thus, the kinetics of $P\bar{v}_{CO_2}$ was examined in the present study.
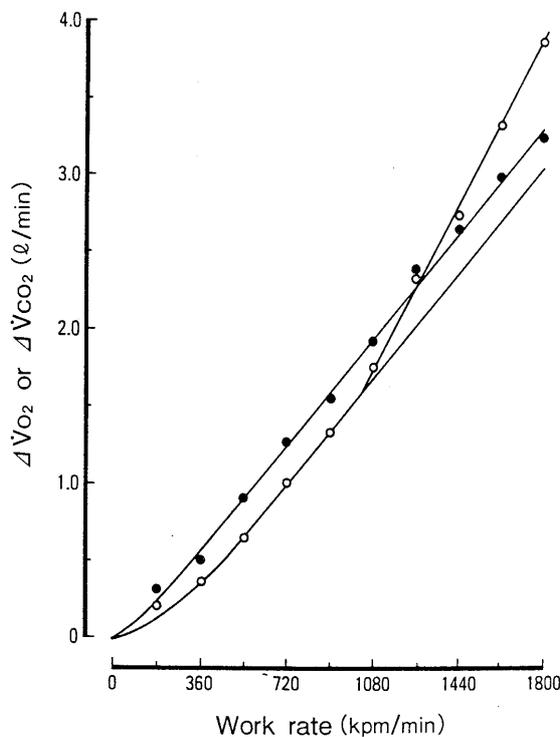
Methods

The subjects were eight trained males belonging to sport clubs of the college. Their age was 21 ± 1.41 yr (mean $\pm$ SD), height 170 ± 4.58 cm, weight 59 ± 4.48 kg, and maximal oxygen uptake 3.52 ± 0.295 l/min. All subjects were informed of the purpose of the experiment, the procedure, and the risks before their consent was obtained.

The exercise was performed using a Monark bicycle ergometer. The work load started from 180 kpm/min and thereafter was increased by 180 kpm/min every minute until the subject could not follow the pedaling rate of 60 rpm (exhaustion test). Two incremental-load exercises up to 540 and 1080 kpm/min were also performed later (submaximal tests).

At the exhaustion test, expired gas was collected for 5 min at rest, and every minute during the exercise with Douglas bags. Then fractions of O_2 and CO_2 in the Douglas bags were analyzed by a Mass spectrometer (Perkin Elma MGA-1100) and the volume was measured by a dry gas meter to give the minute ventilation. From these data, O_2 uptake ($\dot{V}_{O_2}$) and CO_2 output ($\dot{V}_{CO_2}$) were calculated. CO_2 rebreathing (Defares et al., 1961) was performed at rest and immediately after the exhaustion test, and immediately after 540 and 1080 kpm/min of submaximal tests. The rebreathing gas contained 5 % of CO_2 in O_2 balance. The CO_2 pressure obtained from the

CO_2 rebreathing was used to estimate mixed venous CO_2 pressure (detail in Yano et al., 1984). Blood was collected from the median cubital vein at rest and 5 min after the submaximal test up to 1080 kpm/min and exhaustion test, and was analyzed by Lactate Analyzer LA 640 (Roche).

The difference between $\dot{V}o_2$ or $\dot{V}co_2$ in exercise and at rest ($\Delta\dot{V}o_2$ or $\Delta\dot{V}co_2$) is shown in Fig. 1. $\Delta\dot{V}co_2$ indicated a linear increase at low work rate, and this increasing rate changed. Before this changing point, there was a difinite difference between $\Delta\dot{V}o_2$ and $\Delta\dot{V}co_2$ at each work rate. This difference was defined to be the respiratory phase of CO_2 store (stored$\dot{V}co_2$). The regression line between $\Delta\dot{V}co_2$ and the work rate was obtained at the period of linear increase of $\Delta\dot{V}co_2$. This regression line was extrapolated to obtain the prediction of $\Delta\dot{V}co_2$ after the changing point (pred$\dot{V}co_2$). The difference between $\Delta\dot{V}o_2$ and pred$\dot{V}co_2$ was also defined as the stored$\dot{V}co_2$ after the change of rate of increase of $\Delta\dot{V}co_2$. Then stored$\dot{V}co_2$ was added along different lapses. This was defined as the amount of CO_2 store (stored CO_2). Furthermore, the difference between measured $\Delta\dot{V}co_2$ and pred$\dot{V}co_2$ was defined as the respiratory phase of CO_2 excess (excess$\dot{V}co_2$). The added value of excess$\dot{V}co_2$ along different lapses was defined as the amount of excessive CO_2 expiration (excess CO_2).

The relationship between independent and dependent valuables was expressed as the Pearson coefficient of correlation. A significant level was accepted at $p<0.05$.

Results

The excess$\dot{V}co_2$ started from 1080 kpm/min for 3 subjects, 1260 kpm/min for 4 subjects, and 1440 kpm/min for 1 subject. Blood lactate was 1.11 ± 0.16 mM at rest, 1.79 ± 0.66 mM after 1080 kpm/min of submaximal test, and 9.45 ± 1.96 mM after exhaustion test. The difference between blood lactates after exercise and at rest significantly related to excessCO_2 ($r=0.828$, $p<0.001$).

Figure 2 shows the kinetics of stored CO_2 against the rise of work rate. A slope of the linear regression lines obtained between $\Delta\dot{V}co_2$ and work rate was not always the same as increasing rate of $\Delta\dot{V}o_2$. When the slope was steep, stored$\dot{V}co_2$ became small at upper work rate and vice versa. Therefore, estimates were not always excellent, resulting in scatter estimates at high work rate. The stored CO_2 linearly increased against after the delay although stored CO_2 at 720 kpm/min indicated somewhat high value. This delay corresponded to about one minute.

Figure 3 shows the kinetics of $P\bar{v}co_2$ against the rise of work rate. $P\bar{v}co_2$ seemed to indicate a linear increase after a somewhat slow rise at the beginning phase of the incremental-load exercise. The rising rate of $P\bar{v}co_2$ did not change at the starting point of excess$\dot{V}co_2$. The $P\bar{v}co_2$ at exhaustion did not deviate from the straight line obtained between 540 and 1080 kpm/min although a lot of

Fig. 1 The differences between O_2 uptake and CO_2 output in exercise and at rest ($\Delta\dot{V}o_2$ and $\Delta\dot{V}co_2$) are shown against work rate. Filled circles indicate $\Delta\dot{V}o_2$. Circles indicate $\Delta\dot{V}co_2$.
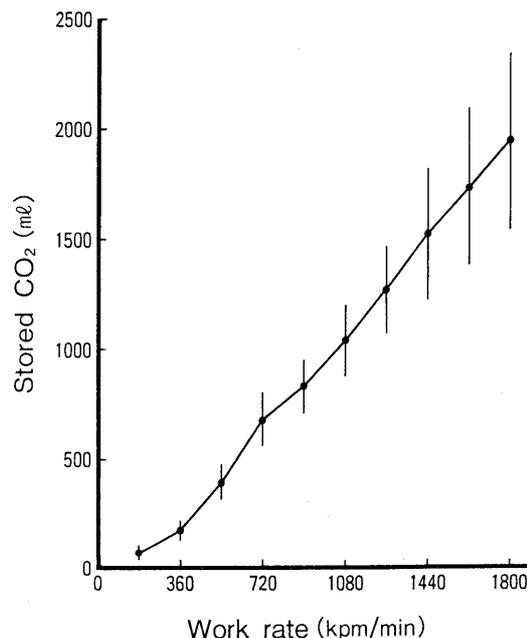

Fig. 2 Kinetics of stored CO_2 during incremental-load exercise. (mean $\pm$ SD)

blood lactate was produced at exhaustion.

When the linear portion of $P\bar{v}co_2$ rise was extrapolated to the lower work rate, $P\bar{v}co_2$ became the value at rest when the work rate was 180 kpm/min corresponding to one minute delay. As this trend of $P\bar{v}co_2$ kinetics was similar to that of stored CO_2, this relationship was examined. As shown in Fig. 4, $P\bar{v}co_2$ significantly related to stored CO_2 (r=0.876, p<0.01).

Discussion

The purpose of the present study was to examine the kinetics of $P\bar{v}co_2$ in incremental-load exercise. $P\bar{v}co_2$ seemed to indicate a linear increase after a somewhat slow increase. Stored CO_2 was calculated from the $\Delta\dot{V}o_2$ and $\Delta\dot{V}co_2$. The stored CO_2 indicated linear increase after a time delay. $P\bar{v}co_2$ significantly related to the stored CO_2. Blood lactate seemed to start to increase at around

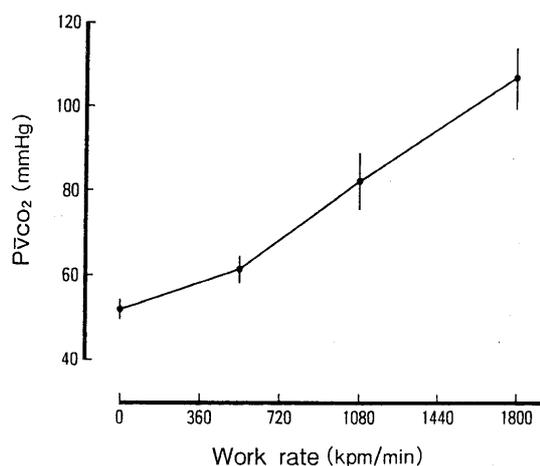**Fig. 3** Kinetics of mixed venous CO_2 pressure ($P\bar{v}co_2$) during incremental-load exercise and at rest. (mean ± SD)

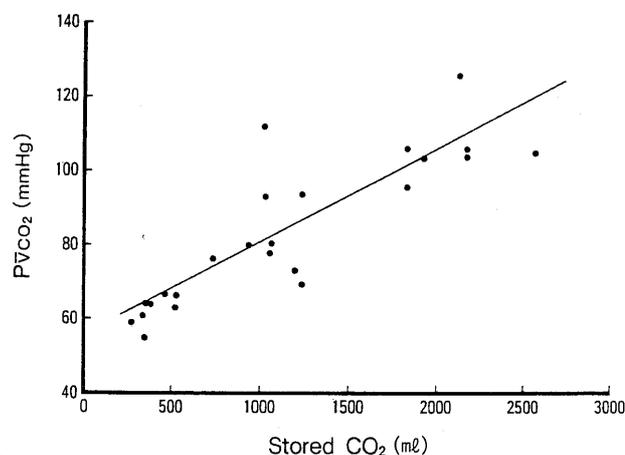**Fig. 4** Relationship between mixed venous CO_2 pressure ($P\bar{v}co_2$) and stored CO_2.

1080 kpm/min. In spite of this changes, the linear increase of $P\bar{v}co_2$ was unchanged. Blood lactate rise significantly related to excess CO_2.

In the present study, stored CO_2 was obtained through the difference between $\Delta\dot{V}o_2$ and $\Delta\dot{V}co_2$. This is because if the absolute values of $\dot{V}o_2$ and $\dot{V}co_2$ were to be used for the calculation of stored $\dot{V}co_2$, the stored CO_2 would be calculated at rest. In order to avoid this contradiction, the difference between $\dot{V}o_2$ and $\dot{V}co_2$ at rest ($\dot{V}o_2$rest − $\dot{V}co_2$rest) is eliminated from $\dot{V}o_2$ during exercise. Its value is, then, assumed to be equal to the CO_2 product ($\dot{V}co_2$prod). That is,

$$\dot{V}co_2prod = \dot{V}o_2 - (\dot{V}o_2rest - \dot{V}co_2rest)$$

As stored$\dot{V}co_2 = \dot{V}co_2prod - \dot{V}co_2$,

$$stored\dot{V}co_2 = \dot{V}o_2 - (\dot{V}o_2rest - \dot{V}co_2rest) - \dot{V}co_2$$
$$= \Delta\dot{V}o_2 - \Delta\dot{V}co_2$$

This is the present way of calculation on stored$\dot{V}co_2$.

As respiratory quotient(RQ) is $\dot{V}co_2prod/\dot{V}o_2$,

$$RQ = (\dot{V}o_2 - (\dot{V}o_2rest - \dot{V}co_2rest))/\dot{V}o_2$$
$$= 1 - (\dot{V}o_2rest - \dot{V}co_2rest)/\dot{V}o_2$$

This equation becomes $\dot{V}co_2rest/\dot{V}o_2rest$ at rest as $\dot{V}o_2$ is equal to $\dot{V}o_2rest$. This is corresponding to respiratory gas exchange ratio (RER) at rest. As $\dot{V}o_2$ increases in exercise, the second term of the equation approaches zero, and RQ approaches from RER (=RQ) at rest to 1.

Thus the storedCO_2 was obtained under these conditions.

The obtained storedCO_2 related to $P\bar{v}co_2$. Therefore, the kinetics of $P\bar{v}co_2$ at light and moderate exercise intensities can be estimated from the storedCO_2. The estimated kinetics of $P\bar{v}co_2$ seems to be a linear increase with a time delay.

In the incremental exercise, it is known that blood lactate starts to increase above a certain work load (Beaver et al., 1986 a, b). This lactic acid is partly buffered by the bicarbonate system (Hultman and Sahlin, 1980; Yano, 1987). In this chemical reaction, the bicarbonate ion shifts toward CO_2. If the shifted CO_2 is not perfectly removed, CO_2 pressure increases. This was predicted particularly in the active muscle producing lactic acid, and the increase of CO_2 pressure in the active muscle could induce the rise of mixed venous CO_2 pressure. However, the effect of lactate increase on $P\bar{v}co_2$ was not confirmed in the present study.

The reason for $P\bar{v}co_2$ being unaffected may relate to the velocity of chemical reaction between CO_2 and bicarbonate ion in bicarbonate buffering system. This velocity is slow in the muscle cell (Sahlin et al., 1978) as the enzyme to catalyze the reaction is inactive. Therefore, the buffer by bicarbonate system does not produce the quick shift toward CO_2. If during this delay the bicarbonate ion is removed from muscle cell, CO_2 in the muscle cell is not increased.

The present study indicated that CO_2 was excessively expired in response to the increase of blood lactate.

Unless the obtained excessCO_2 included an amount of the bicarbonate ion removed from active muscle cell, CO_2 pressure in the active muscle cell, consequently $P\bar{v}CO_2$ could have been affected.

Thus, within the present results and assumptions it seemed that $P\bar{v}CO_2$ indicated a linear increase with a time delay without the effect of lactate increase in incremental-load exercise.

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